DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
Rockville, MD 20857

NDA 20-845/S-002

INO Therapeutics, Inc.
Attention: Ms. Mary Ellen Zamstein
6 State Route 173
Clinton, NJ 08809

Dear Ms. Zamstein:

Please refer to your supplemental new drug application dated January 23, 2004 submitted under section 505(b) of the Federal Food, Drug, and Cosmetic Act for INOmax (nitric oxide) for inhalation.

We acknowledge receipt of your submission dated April 23, 2004.

This "Changes Being Effected in 30 days" supplemental new drug application provides for final printed labeling revised as follows:

1. The **Drug Interactions** section has been revised, and now reads as follows:

   Drug Interactions
   No formal drug-interaction studies have been performed, and a clinically significant interaction with other medications used in the treatment of hypoxic respiratory failure cannot be excluded based on the available data. INOmax has been administered with tolazoline, dopamine, dobutamine, steroids, surfactant, and high-frequency ventilation. Although there are no study data to evaluate the possibility, nitric oxide donor compounds, including sodium nitroprusside and nitroglycerin, may have an additive effect with INOmax on the risk of developing methemoglobinemia. An association between prilocaine and an increased risk of methaemoglobinaemia, particularly in infants, has specifically been described in a literature case report. This risk is present whether the drugs are administered as oral, parenteral, or topical formulations.

2. The word "study" has been added after "NINOS" in the forth paragraph of the **ADVERSE REACTIONS** section.

3. A new **POST-MARKETING EXPERIENCE** section has been added after the **OVERDOSAGE** section that reads as follows:

   POST-MARKETING EXPERIENCE

   The following adverse events have been reported as part of the post-marketing surveillance. These events have not been reported above. Given the nature of spontaneously reported post-marketing surveillance data, it is impossible to determine the actual incidence of the events or definitively establish their causal relationship to the drug. The listing is alphabetical: dose errors associated with the delivery system; headaches associated with environmental exposure of INOmax in hospital staff; hypotension associate with acute withdrawal of the drug; hypoxemia associated with acute withdrawal of the drug; pulmonary edema in patients with CREST syndrome.

4. At the end of the labeling, the corporate name "INO Therapeutics, Inc" has been changed to "INO Therapeutics."

We have completed our review of this supplemental new drug application. It is approved, effective on the date of this letter, for use as recommended in the final printed labeling (FPL) submitted on April 23, 2004.

If you issue a letter communicating important information about this drug product (i.e., a "Dear Health Care Professional" letter), we request that you submit a copy of the letter to this NDA and a copy to the following address:

MEDWATCH, HFD-410
FDA
5600 Fishers Lane
Rockville, MD 20857

We remind you that you must comply with the requirements for an approved NDA set forth under 21 CFR 314.80 and 314.81.

If you have any questions, please contact:

Mr. Russell Fortney
Regulatory Health Project Manager
(301) 594-5311

Sincerely,

{See appended electronic signature page}

Norman Stockbridge, M.D., Ph.D.
Acting Director
Division of Cardio-Renal Drug Products
Office of Drug Evaluation I
Center for Drug Evaluation and Research

This is a representation of an electronic record that was signed electronically and this page is the manifestation of the electronic signature.

/s/

Norman Stockbridge

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